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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,836	08/19/2003	Jean-Baptiste Dumas Milne Edwards	G-078US05DIV	4906

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 06/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,836	DUMAS MILNE EDWARDS ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover she t with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-26 are pending.

Applicants' amendment and Declaration of Frank Christopher Eisenschenk filed March 22, 2006 are acknowledged. Applicant's response has been fully considered. Claims 1 and 9 have been amended, and new claims 17-26 have been added. Therefore, claims 1-26 are examined.

Withdrawn Informalities

2. The previous objection to the specification regarding embedded hyperlinks and amino acid residue 112 of SEQ ID NO:297 is withdrawn in view of applicant's amendment to the specification, and applicants' response at page 8 in the amendment filed March 22, 2006.

Withdrawn Claim Rejections - 35 USC § 112

3. The previous rejection of claims 3 and 11 under 35 U. S. C. 112, first paragraph, regarding the deposited clones, is withdrawn in view of Declaration of Frank Christopher Eisenschenk, receipt of the deposit, and applicants' response at pages 11-12 in the amendment filed March 22, 2006.

Maintained Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Previous rejection of claims 1-16 under 35 U.S.C. 101 is maintained, and new claims 17-26 have been added to the rejection because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1-26 are directed to an isolated polypeptide comprising an amino acid sequence at least 95%, 96%, 97%, 98% or 99% identical to the amino acid sequence of SEQ ID NO:297 or a composition comprising the polypeptide. The polypeptide of SEQ ID NO:297 is disclosed as a splice variant of synaptogyrin 1 and is identical to synaptogyrin 1 up to amino acid residue 112, where the protein of SEQ ID NO:297 has the same N-terminal domain (1-16 residues) and 2 of 4 transmembrane helices. The specification indicates the protein of the invention such as SEQ ID NO:297 or its related protein is believed to be a member of the synaptogyrin family because the polypeptides of the invention comprise the same N-terminal cytoplasmic domain (residues 1-16) of the synaptogyrin protein, which is highly conserved among all the members of synaptogyrin family (Fig. 6 of Kedra et al., Human Genetics 103, 131-141 (1998)); and the polypeptides of the invention also comprise amino acids 25-45 and/or 68-88, which are the two transmembrane alpha helices in the synaptogyrin protein (page 280, line 21 to page 281, line 2 of the specification). The specification also indicates that synaptogyrins are closely related to proteins of the synaptophysin family, both of which are involved in neurotransmission and more generally exocytosis and vesicle trafficking (page 281, lines 3-11), and the normal function and organization of eukaryotic cells is dependent on the transport of various vesicles that selectively shuttle membrane and cargo between distinct compartments of the secretory and endocytotic pathways, where numerous human diseases can be attributed to defects in the trafficking of proteins to organelles or the cell surfaces (page 281, line 12- page 282, line 14). Thus, the

protein of the invention can be used to diagnose, treat, and prevent any disorder in which trafficking or the fusion machinery is affected (pages 282-284). It appears that SEQ ID NO:297 or its related protein being identified as a member of synaptogyrin family is based on the comparison of SEQ ID NO:297 (132 amino acids) with synaptogyrin 1 (234 amino acids), which indicates the protein of SEQ ID NO:297 has the same N-terminal domain and 2 of 4 transmembrane helices, however, the members of synaptogyrin family (e.g., SYNGR1b, 191 amino acids; SYNGR1c, 192 amino acids) have central portions of the proteins (residues 34-161) strongly conserved and four membrane-spanning helices (Fig. 6, and pages 137-138 of Kedra et al., 1998), while the protein of SEQ ID NO:297 only contains 132 amino acids, a portion of the conserved region in the synaptogyrin protein (1-112 residues) and a C-terminal domain of 20 amino acids, which is different from other synaptogyrin proteins. Thus, without further experimentation to indicate the protein of SEQ ID NO:297 having the biological activity in vesicle trafficking, it is not known whether SEQ ID NO:297 or it related protein is a functional synaptogyrin protein. Since the biological role of SEQ ID NO:297 or its related protein as a synaptogyrin protein has not been established, the claimed polypeptides do not have the utility as a synaptogyrin protein. For these reasons, the instant invention does not possess a specific or a well-established utility, although there is a general utility that is applicable to the broad class of synaptogyrin proteins. The utility is not a substantial utility because it requires further research to identify or reasonably confirm a "real world" context of use. Basic research to characterize the claimed invention, use in an assay to identify modulators of the instant invention, or production of antibodies to identify other related proteins do not constitute substantial utilities.

Response to Arguments

Applicants indicate the utility of the claimed invention does not turn on whether its function has been demonstrated in the specification. Rather, the test is whether the claimed polypeptide has the functions asserted in the specification and can be used for the purposes set forth therein; regarding the transmembrane helices, it can only be concluded that rat synaptogyrin spans the membrane four times in view of Kedra et al. For human synaptogyrins, the structure is only based on a prediction using the PredictProtein program (see page 13, right column, lines 11-14 of Kedra et al.), however, the accuracy of this prediction cannot be ascertained. For example, using another prediction program, i.e., the TMHMM program, human synaptogyrin lc of Kedra et al. is predicted to span the membrane three times and not the four times as predicted by Kedra et al. (see Appendix 1). Thus, a synaptogyrin splice variant taught to span the membrane two times does not allow for the conclusion that a splice variant is not a functional synaptogyrin simply in view of Kedra et al. and the arguments set forth in the office Action; in Appendix 2, the synaptogyrin splice variant of the present invention displays many characteristic features that are common to all members of the synaptogyrin family and previously noted in the Office Action (see page 3). Thus, one of skill in the art would conclude it is more likely than not that the synaptogyrin splice variant of the present invention is a functional synaptogyrin particularly in view of Kedra et al. Applicants also indicate one skilled in the art would have known how to use the claimed invention in view of the teachings of the specification, e.g., to use the claimed polypeptide as marker protein (see page 62, lines 8-12); to identify secretory and endocytic traffic in cells (see page 282, lines 15-16); or to use the claimed polypeptide for targeting of heterologous polypeptides or polynucleotides to components of the

secretory machinery (page 282, lines 24-27). In view of the analysis, one skilled in the art would have concluded the claimed polypeptide have credible, specific and substantial utilities (pages 8-10 of the response).

Applicants' response has been considered, however, the arguments are not found persuasive because of the following reasons. Although the protein of SEQ ID NO:297 has several characteristic features (i.e., the N-terminal domain, 1-16 residues; 2 of 4 transmembrane helices; a disulfide bond between the first and second transmembrane domains) that are common to all members of the synaptogyrin family, the protein of SEQ ID NO:297 also has some different structural features from other members of synaptogyrin family. For example, while the members of synaptogyrin family have central portions of the proteins (residues 34-161) strongly conserved and four membrane-spanning helices (Fig. 6, and pages 137-138 of Kedra et al., 1998), the protein of SEQ ID NO:297 only contains 132 amino acids, a portion of the conserved region in the synaptogyrin protein (1-112 residues) and a C-terminal functional domain of 20 amino acids, which is different from other synaptogyrin proteins. Since the protein of SEQ ID NO:297 is structurally different from other members of synaptogyrin family in terms of C-terminal functional domain and transmembrane helices in the central conserved region, and the specification has not established the protein of SEQ ID NO:297 is a functional synaptogyrin protein, it would require further experimentation to show the claimed protein being a functional synaptogyrin protein and to identify or reasonably confirm a "real world" context of use. Regarding the number of transmembrane helices, the protein of SEQ ID NO:297 only has two transmembrane helices as predicted by the TMHMM program (see Appendix 1) since it only contains part of central conserved region (residues 34-122), while other members of

synaptogyrin family have 3 or 4 transmembrane helices as predicted by the TMHMM program (see Appendix 1) or the PredictProtein program (Kedra et al.). Regarding the use of the claimed protein as a marker protein to identify secretory and endocytic traffic in cells, or the use of claimed protein to target heterologous polypeptides or polynucleotides to components of the secretory machinery, which is applicable only if the function of the claimed protein is established.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-26 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

5. Previous rejection of claims 1-3, 5, 7, 9-11, 13, 15 (mistakenly as claims 1-5, 7, 9-13 and 15 at the beginning of paragraph 5 in previous Office Action) under 35 U.S.C. 112, first paragraph is maintained, and new claims 17-26 have been added to the rejection as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 5, 7, 9-11, 13, 15 and 17-26 are directed to an isolated polypeptide comprising an amino acid sequence at least 95%, 96%, 97%, 98% or 99% identical to the amino

acid sequence of SEQ ID NO:297, where the polypeptide may play a role in vesicle trafficking. The specification discloses the protein of SEQ ID NO:297 is a splice variant of synaptogyrin 1 and is identical to synaptogyrin 1 up to amino acid residue 112, where the protein of SEQ ID NO:297 has the same N-terminal domain and 2 of 4 transmembrane helixes; synnaptogyrins are closely related to proteins of the synaptophysin family, both of which are involved in neurotransmission and more generally exocytosis and vesicle trafficking (page 280, line 21-to page 281, line 11); and a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% (5 of 100) of the amino acid residues in the subject sequence may be inserted, deleted, or substituted with another amino acid (page 51, line 25-page 52, line 4). However, the specification does not identify the amino acid residues that are essential to the function of the polypeptide, and how to identify a functional peptide. Furthermore, there is no disclosure of any particular structure to function/activity relationship in the disclosed species (i.e., polypeptides comprising amino acid sequences at least 95% identical to SEQ ID NO:297). Without guidance on structure to function/activity of the claimed polypeptides, one skilled in the art would not know which portions or fragments of the sequence are essential for function/activity, and how to produce a functional polypeptide. The lack of description on the structure to function/activity relationship of the polypeptides, and the lack of representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Response to Arguments

Applicants indicate the written description requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." The specification teaches a 134 amino acid splice variant of synaptogyrin (SEQ ID NO: 297), the first 112 amino acids of the claimed polypeptide are identical to synaptogyrin 1, various domains of the claimed polypeptide (e.g., transmembrane domains), and the claimed polypeptides has the same N-terminal domain which is highly conserved in all synaptogyrins. Thus, the specification teaches the particular structure of the claimed polypeptides as well as various domain identified within SEQ ID NO: 297. Kedra et al. disclose a number of highly conserved regions among the synaptogyrins (see paragraph bridging columns 1-2, page 138). There are no more than about six to seven amino acid changes embraced by the claims and those skilled in the art would have recognized those domains in which substitutions would be tolerated without adversely affecting the biological function of the claimed polypeptide (page 64, lines 23-26, conservative amino acid substitutions in transmembrsne domains) and those domains in which no substitutions should be made (e.g., amino acids 1-16 or 1-33, highly conserved amino acids among the members of the synaptogyrin family). In view of such facts, the claimed invention satisfies the written description requirement (pages 10-11 of the response).

Applicants' response has been considered, however, the arguments are not found persuasive because of the following reasons. Although the specification disclose some structural features of the claimed polypeptide, it does not indicate where the changes (which residues) or what changes (substitution, deletion or addition) are made to the sequences that are at least 95% identical to the protein of SEQ ID NO:297, and what effect the changes of the sequence would

have. Furthermore, there are no teachings on structure to function/activity relationship and no sequences having at least 95% sequence identity to SEQ ID NO:297 are identified as functional synaptogyrin proteins. Therefore, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Conclusion

6. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CHIH-MIN KAM
PATENT EXAMINER

CMK
June 2, 2006